

ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

ahfmr research news

SPRING 2004



On the Cover



Graham Johnson is an Edmontonian and a graduate of the Grant MacEwan College Visual Communication Design program. He currently works as a graphic designer and illustrator. The cover art is acrylic on Canvas.

AHFMR Mission

AHFMR supports a community of researchers who generate knowledge whose application improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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6 The obesity epidemic

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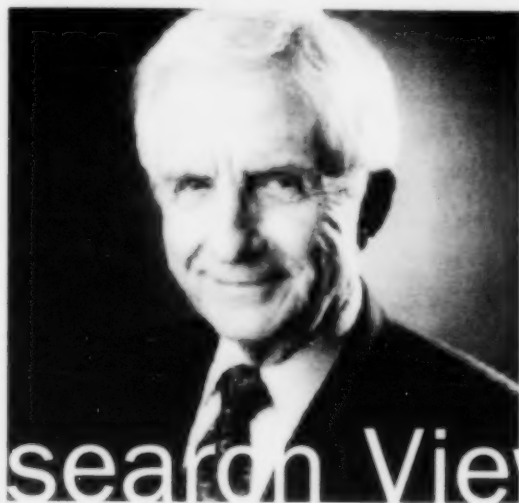
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search View

Come July 2004, Dr. Matthew Spence will be on his motorcycle. "I'm not sure where I'll be heading yet, but that is the plan—the open road and my motorcycle," he says.

After 14 years at the helm of AHFMR, Dr. Spence, president and CEO, is retiring. A lot has changed in those years. Dr. Spence compares the Foundation he inherited in 1990 to an accomplished adolescent with tremendous promise but still growing and maturing. Now, like many 24-year-olds, AHFMR has a better sense of self and of the surrounding world—and faces an even more brilliant future.

"Over the years the research environment has become much more complex," says Dr. Spence. "It has become a much larger activity, not only in Alberta, but around the world." He points out that constantly improving methods of communication and new breakthroughs in science have made the research world even more collaborative and more global. "And as the research world has changed, so has the Foundation, partly in response to

that external change, but also in an effort to lead it." During his tenure, AHFMR has strengthened its basic biomedical and clinical research programs, put its

Technology Commercialization program on a strong footing, and started a series of health research programs.

"It's been enormously rewarding to work with 'can-do' people with such vision—people at the provincial government level, at the universities themselves, throughout the research community, the public, and here at AHFMR," he adds. "When I travel around the world and look at how research is being done, I come back with the feeling that this is one of the best places in the world."

And it keeps getting better. "Predicting directions for research is always hazardous, because you're never quite sure what's around the corner," cautions Dr. Spence. "But I think I can make a couple of unqualified

"It's been enormously rewarding work."

"The fun all the way along has been meeting so many very bright people."

statements: research in Alberta is going to get steadily better. And it's going to get more and more multidisciplinary and interdisciplinary; in other words, crossing traditional boundaries and borders, and using skills and techniques from a variety of other areas. We're already starting to use more and more of the social scientist's skills in the biological and clinical areas.

"I think we also have a great opportunity in this province to create great teaching and research health regions, in addition to having great teaching and research institutions. We have a regional health system that can become a world-leading research and teaching resource—it's a true opportunity for this province. To establish more health research on a regional footing, as opposed to solely in a single faculty or school. We can take advantage of the fact that we have this integrated system by using it to study disease and health over the population, and to put models in place that are really not possible in most other places. My dream in helping to establish the SEARCH program was that Alberta would become a natural laboratory from border to border—that no matter where you went in this province, you would find people creating, collecting, and using health-research evidence. And because of that, others would beat a path to our doors. I think that's coming."



What has Dr. Spence most enjoyed about the job? "The fun all the way along has been meeting so many very bright people—the researchers and trainees that we support," he answers immediately. "They are full of ideas, enthusiastic, and grateful for the opportunities we have provided. I find it a real thrill. One of my few disappointments moving into this position has been that I could not stay active in research myself, so I get a kind of vicarious pleasure out of meeting these people. I enjoy hearing about the science so much, and I pride myself that sometimes I understand parts of it! In a sense, the Foundation basks in the reflected glory of the investigators."

His only advice for his successor, Dr. Kevin Keough: value the quality of people you work with, keep a sense of humour, and don't take yourself too seriously.

Post-AHFMR, Dr. Spence also plans to catch up on other activities, including some of the reading he has put off for an awfully long time. "Let me put it this way: I've been a clinician-investigator most of my life, and I see myself continuing to investigate life when I retire." ■

THE fitne

The dreaded "Freshman 15".

It's the notion that first-year college or university students can expect to gain about 15 pounds by the end of the school year through lack of exercise and bad eating habits.

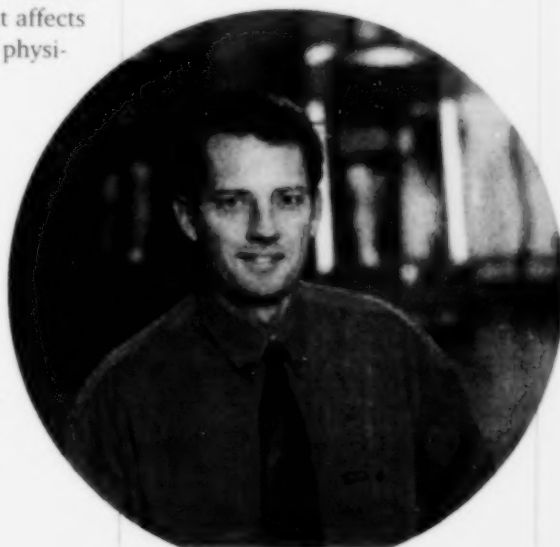
While the 15-pound weight gain may be an exaggeration, the drop in physical-activity levels in first-year students is real. University of Lethbridge researcher Dr. Steven Bray wants to know why. Physical activity peaks in early adolescence, then declines sharply from late adolescence, and continues its downward trend through older adulthood. With support from the Health Research Fund, Dr. Bray is examining what happens during this transition to college or university that affects young people's levels of physical activity.

"Clearly, part of the answer is that young people were getting some of their physical activity through the high-school curriculum," says Dr. Bray. His original pilot project surveyed 150 University of Lethbridge students and found that about 65% were active

"The transition from high school to college or university is a very difficult one."

enough (according to the Canada Physical Activity Guide) in high school, but in their first year of post-secondary education their level of activity dropped to 40% of what it had

been. "The transition from high school to college or university is a very difficult one, especially for students who are leaving home and living on their own for the first time. This study gives us an opportunity to actually look at what is going on, and also to see




ss habit

fit



"The physical-activity routines students get themselves into become quite important habits."

or university were still active five years later, and 85% of those who were inactive had remained inactive. "We're learning that the physical-activity routines students get themselves into become quite important habits," says Dr. Bray. "And active individuals tend to promote active lifestyles to those with whom they come into contact."

In partnership with the Alberta Centre for Active Living in Edmonton, Dr. Bray will circulate his findings through the centre's Be Fit for Life Network, which is funded by Alberta Community Development. Ultimately he would like to provide those students whose levels of activity are decreasing with some strategies for preserving physical activity. Getting first-year students active from the very beginning might make a difference in years to come. "My research differs from a typical physical-activity intervention," he adds. "Rather than getting sedentary people to start exercising, I'm trying to preserve the activity levels of young people who are already active." 

what those students who stay active are doing differently from those who do not."

Dr. Bray is building on his pilot study and surveying about 1000 first-year students at the University of Lethbridge and Lethbridge Community College. In September the students gave an account of their physical activity over the previous eight months, with follow-ups in November and March to show activity levels over their first year. Previous data have shown that students tend to become less and less active as they continue through post-secondary education. However, a US study found that 85% of those who were active in their final year of college

Dr. Steven Bray's research is supported by the Health Research Fund, which is administered by AHFMR on behalf of Alberta Health and Wellness; he also receives funding from the Social Sciences and Humanities Research Council of Canada (SSHRC). Dr. Bray is an assistant professor in the Department of Kinesiology at the University of Lethbridge.

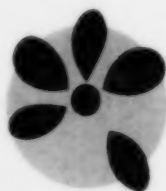
Selected publications

Bray SR, Born HA. Transition to university and vigorous physical activity: Implications for health and psychological well-being. *Journal of American College Health* 2004;52(4): 181-188.

Gyurcsik NC, Bray SR, Brittain DR. Coping with barriers to vigorous physical activity during transition to university. *Family and Community Health*. In press 2004.

Fighting cancer

w i t h f i t n e s s



Most of us know the many benefits of physical activity by now: improved cardiovascular endurance, lower blood pressure, reduced depression and anxiety, and improved self-esteem and body image, to name a few. But despite these benefits, working out or going for a brisk walk is often the last thing people coping with cancer want to do.

The initial shock of the diagnosis, in addition to coping with chemotherapy, radiation, or surgery, can shatter cancer patients' sense of control over their own bodies, explains Dr. Nicole Culos-Reed, a Heritage Population Health Investigator. Farther down the road, they face more challenges in getting regular exercise: debilitating fatigue can last up to five years after treatment; and psychological barriers, including stress and depression, can be overwhelming. "What we're really interested in is giving them back a sense of control of their lives that has been diminished by this cancer diagnosis and treatment and, by doing that, improving their overall quality of life," she says.

Dr. Culos-Reed's AHFMR-funded research investigates the effects of physical activity in cancer survivors. Her study focuses on patients who have completed their main treatment but may be on long-term therapy, such as hormone supplements.

Most research on physical activity and cancer has involved breast cancer patients. Dr. Culos-Reed's study also includes men treated for prostate cancer—

a relatively new area of research. "They're an older population, and they don't have the support groups that breast cancer survivors have," she says. She hopes that regular exercise will prevent or slow the loss of bone mineral density (which can lead to osteoporosis) seen in prostate cancer survivors on long-term hormone therapy.

Dr. Culos-Reed's initial 16-week study in a proposed three-year research program involves two groups of cancer survivors, most of them recruited through the Alberta Cancer Registry. One randomly selected group of about 40 participants is enrolled in a structured, goal-oriented physical activity program. Once a week men and women meet in separate groups for two hours of progressive exercises, using large physiotherapy balls and stretchy bands that work the upper and lower body. Fitter

Working out is often the last thing people coping with cancer want to do.

International Inc. in Calgary donated all the exercise equipment, and the

Talisman Centre for wellness and sport, along with the University of Calgary, provided the space. Instructors in the weekly "booster group" sessions provide participants with new exercises and education to challenge them.

"The weekly session where everyone gets together also serves as a really important group for social support," Dr. Culos-Reed says. "It's just amazing, the bonding that happens in these groups—especially with the men with prostate cancer, because they don't have other people to talk with and do things with."

Tom Mugridge, who has had surgery for prostate cancer and is on long-term hormone therapy, says he would not be getting regular exercise without the support of the group program. "It really does make a difference," says Mugridge, 62, who makes time to fit the program into his busy days as a federal weights and measures inspector. "We have the interaction of hearing how other people are coping, and we try to encourage each other to exert ourselves a little bit more when we're doing the exercises."

At home, participants continue with regular exercise throughout the week and keep a daily log of their activities. "Our primary goal is not just to get them to be active for 16 weeks, but really to initiate the change in their lifestyle so that they incorporate physical activity in their daily lives," says Dr. Culos-Reed.

The study also includes a separate control group of nearly 40 cancer survivors who are on a waiting list for the structured program. Before and after the 16-week study, the active and control groups are given a battery of fitness tests and demographic questions, as well as a questionnaire to measure

"The weekly session serves as a really important group for social support"

each participant's level of stress, depression, and

perceived "self-efficacy" (sense of personal control). Dr. Culos-Reed's research team will follow up with participants for two years after the program ends, including monthly "reminder" sessions, to encourage them to keep physically active.

Dr. Culos-Reed envisions a network of various physical-activity programs and exercise locations for cancer survivors, both adults and children. The potential benefits of this would be huge, she notes, given the estimated 1500 to 2000 new cases of cancer (mostly breast, prostate, and colorectal) seen at the Tom Baker Cancer Centre in any given six-month period. "My ultimate goal with this whole program is that as soon as someone is diagnosed, they get a pamphlet from us that says, 'Here are all your options for physical activity in Calgary.'"

Dr. Culos-Reed began focusing on the benefits of physical activity for specific population groups in her Ph.D. thesis on exercise and fibromyalgia at the University of Waterloo. After she arrived at the University of Calgary in January 2001, Dr. Kerry Courneya (from the University of Alberta's Faculty of Physical Education) and Dr. Barry Bultz (director of the Department of Psychosocial Resources at the Tom Baker Cancer Centre) encouraged her to pursue further research in the area. Dr. Culos-Reed says physical activity has always played an important part in her life, from being an active child to playing high-school sports to becoming a wife and mother in a family that shares a very active lifestyle. Given the many benefits of regular exercise, she says, being inactive "is just not an option".

Dr. Nicole Culos-Reed is an AHFMR Population Health Investigator, an assistant professor in the University of Calgary's Faculty of Kinesiology, an adjunct assistant professor in the Faculty of Medicine's Department of Oncology, and a clinical research associate at the Tom Baker Cancer Centre. In addition to AHFMR funding, her earlier work in this area received support from the Calgary Health Region and the University of Calgary.

Selected publications

Brawley LR, Culos-Reed SN, Angove J, Hoi J, van-Goetz L. Understanding the barriers to physical activity for cancer patients: review and recommendations. *Journal of Psychosocial Oncology* 2002;20(4):1-22.

Culos-Reed SN. Physical activity and cancer in youth: a review of physical activity's protective and rehabilitative functions. *Pediatric Exercise Science* 2002;14:248-258.



LEFT DR NICOLE CULOS REED

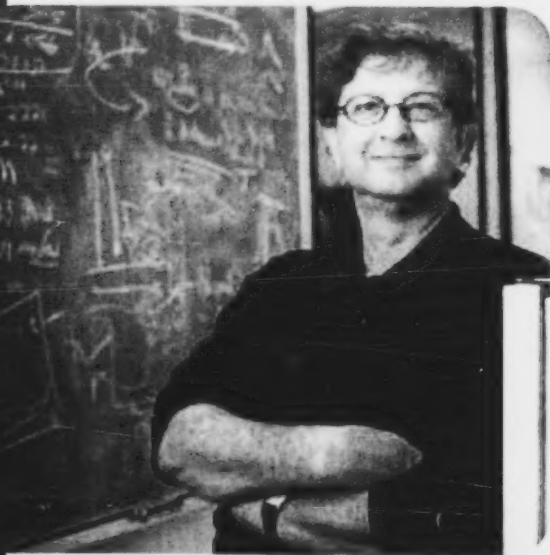
Most people report their weight loss in terms of pounds or inches,

but Louise Denys had a more graphic demonstration:

six garbage bags full of clothes that no longer fitted her. They were the happy results of a successful weight-loss program that saw the 44-year-old Edmonton mother of three children lose 40 pounds in five months.

"A friend and I had been talking about how the pounds had crept on over the years. We decided to do something about it. With my family history, I knew my weight was putting me at risk for heart disease and diabetes. But the truth is, I just wanted to look better."

"Now I feel better too. My blood pressure has dropped significantly; my knee joints don't hurt as much; I have more confidence. And shopping is way more fun! Instead of choosing something that doesn't make me look fat, I'm choosing clothes that make me look good."



The problem is, Louise's experience is not typical.

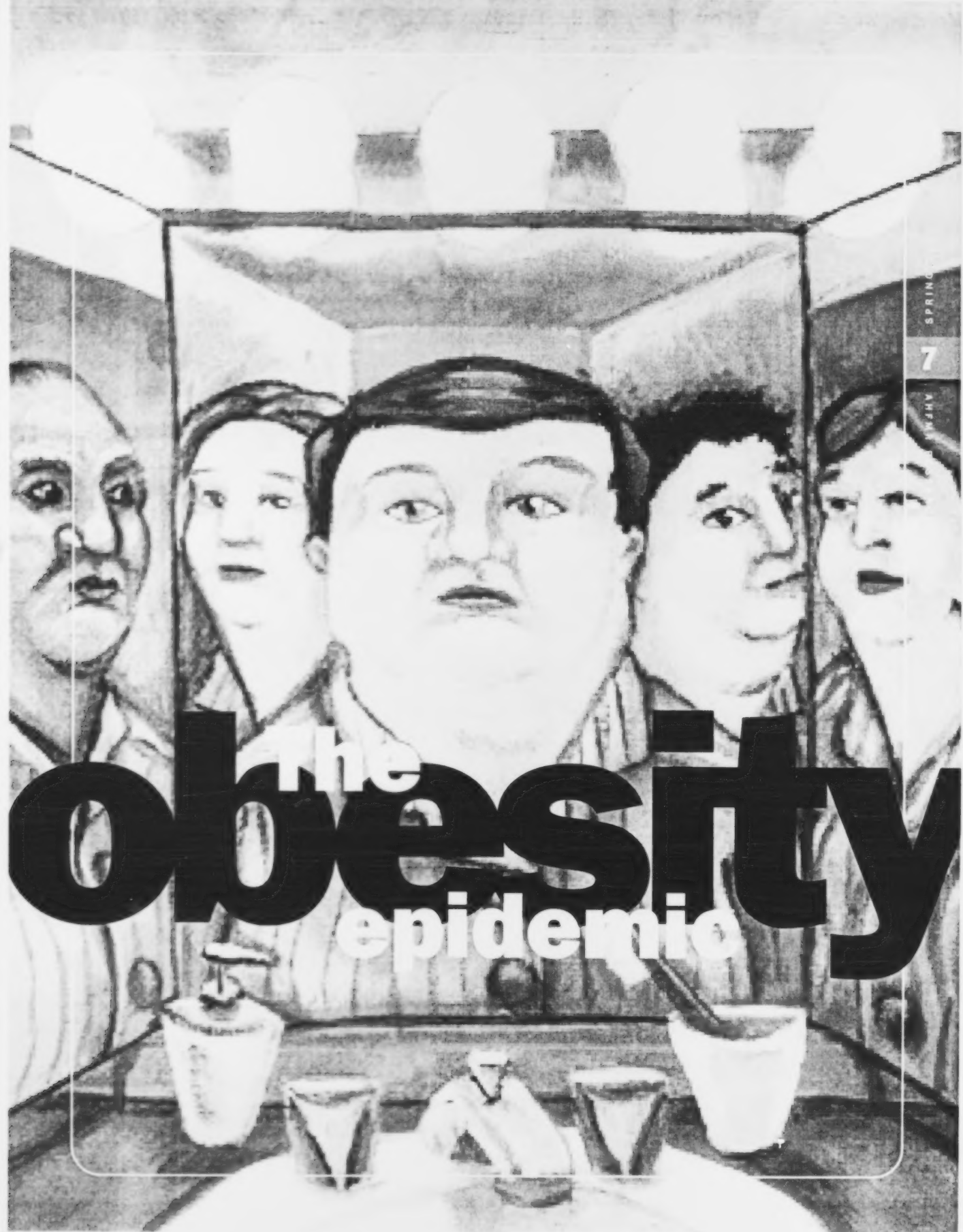
Obesity in Canada has reached crisis proportions, according to a 2004 study by the Heart and Stroke Foundation of Canada. Since the early 1970s, obesity—defined as a body mass index (BMI) of 30 or greater—has jumped by 50% in people aged 20 to 64. More than half of Canadians are overweight (BMI between 25.0 and 29.9) or obese. The Heart and Stroke Foundation calls fat "the new tobacco" because of the huge public health risk. The fatter people are, the more susceptible they are to diabetes, high blood pressure, heart disease, and stroke.

Of course, many people try to do something about their weight. The risks of obesity are well publicized—newspapers, magazines, and television are full of news about diet and exercise. So why do we keep getting fat?

It's a complex issue likely involving genetics, biochemistry, social pressures, environmental situations, and cultural changes. In Alberta, researchers are studying obesity on all these fronts. So far there's no magic cure, only tantalizing clues that may help us win the battle of the bulge someday.

Take the research done by Heritage Scientist Dr. William Colmers, a pharmacology professor at the University of Alberta. Dr. Colmers studies how the brain regulates appetite. According to conventional wisdom, he explains, we get fat because of an excess of intake over output of calories, and the

The obesity epidemic



The epidemic

There are relatively few "stop eating" signals.

excess is stored as fat. "But I'm interested in finding out why there is an imbalance in the first place. Why aren't we sensing that we're full?"

There are many signals (sent using such messengers as hormones and neurotransmitters) that tell the brain we're hungry. Interestingly, there are relatively few "stop eating" signals. The reason could lie in our past. No species of animal—humans included—has evolved in an environment where there was excess food. Consequently, there has never been much need for a stop signal. Only recently have we been living with an abundance of tasty, high-energy foods—and we don't have the chemical messengers to help us cope with that situation.

Dr. Colmers is known for his detailed studies on chemical messengers in the brain. He was part of an international team which discovered that a hormone called ghrelin is one of the main chemical messengers linked to the urge to eat. Dr. Colmers played a key role in figuring out what ghrelin does in the brain, including identifying the receptors it binds to and the relationships it has with other messengers. This work opens up the possibility of designing drugs to target and block hunger.

But there's still a lot to learn, cautions Dr. Colmers. "It's a complex pathway that eventually leads us to think we're hungry, with probably seven or eight major players in the hunger message, which do other things as well." His CIHR-funded New Emerging Team (NET) on the Neurobiology of Obesity—which includes scientists from the University of Calgary, Queen's University, and Université Laval—will study these factors to identify the most promising targets. "The real challenge will be to find treatments that modify appetite without messing up other important systems in the body."

Fat metabolism

Another University of Alberta scientist, Heritage Scholar Dr. Richard Lehner, looks at what happens after we have processed those hunger messages. His



TGH plays a role in secreting fat into the bloodstream.

specialty is fat metabolism, and his team has discovered an enzyme—TGH (triacylglycerol hydrolase)—that plays an important role in fat metabolism.

"This enzyme is active in the 'axis of evil' of fat metabolism: the intestine, the liver, and the adipose [fatty] tissue," says Dr. Lehner. TGH plays a role in secreting fat from these three locations into the bloodstream. Dr. Lehner's team has managed to inhibit TGH in experiments in cell cultures, and they are now doing similar work in mice. The research is done in partnership with the GlaxoSmithKline pharmaceutical company.

"The idea is that by inhibiting TGH, fat does not get into the bloodstream and deposited in the tissues," Dr. Lehner notes. "A drug that works this way could be very valuable for those who are genetically obese and those with adult-onset diabetes, although it wouldn't be a magic bullet for everyone who is overweight."

"It's exciting to be doing research that is directly related to a health problem. That's why I got into research in the first place. It's gratifying to see basic research—which is not quick to do—have clinical applications."

Recently, Dr. Lehner has added another enzyme to his "hit list", one involved in triglyceride synthesis. Triglycerides are a form of fat carried through the bloodstream, and fat has to be made into triglycerides to get out of the cells. Any enzyme

involved in this transformation is a potential target for the inhibition of triglyceride synthesis.

"We're still in the early stages of this work. Fat absorption has turned out to be much more complex than was once thought. But that's okay, because the complexity means we have a number of interesting targets."

Fatty acids

But don't think that fat is all bad, says Heritage Senior Scholar Dr. Luc Berthiaume. "It's just that too much fat is bad. Fats inside our cells are absolutely vital as a source of energy and for several aspects of cellular structure, signalling, and metabolic regulation," he explains. Dr. Berthiaume is referring to protein lipidation, a process whereby a fat molecule attaches to a protein and alters its function. In his University of Alberta lab he studies a particular kind of protein lipidation in which the proteins are modified by fatty acids, a process called fatty acylation. The research has potential applications in treating obesity, heart disease, and cancer.

The study of fatty acylation is relatively new, and was in its infancy when Dr. Berthiaume began his post-doctoral research 12 years ago. "Investigating how this new control mechanism works at the molecular level is imperative," he says.

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Am I overweight ?

In 2003 Health Canada released a revised body-weight classification system for Canadian adults. It categorizes health risk according to (a) body weight, as measured by the body mass index (BMI); and (b) level of abdominal fat, as measured by waist circumference. The system is intended for use among Canadian adults aged 18 years and older, except pregnant and lactating women.

Measuring BMI: Take your weight in kilograms (wearing light clothing and no shoes), and your height in metres. Record weight to the nearest 0.2 kilogram; height to the nearest 0.5 centimetre. Then use this equation to calculate BMI:

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)} \times \text{height (m)}}$$

Example: For someone 1.70 metres tall who weighs 80 kilograms: $\text{BMI} = 80 = 27.7$
 1.70×1.70

The following ranges of BMI are used to identify levels of health risk:

<18.5	Underweight	Increased risk
18.5-24.9	Normal weight	Least risk
25.0-29.9	Overweight	Increased risk
30 and over	Obese	High to extremely high risk

Measuring waist circumference: While standing, measure at the part of the trunk located midway between the bottom of the lower rib and the top of the pelvic bone. Fit the tape snugly around the body, without compressing the underlying soft tissue. The waist should be measured to the nearest 0.5 centimetre.

Waist measurements are used to identify health risk associated with excess abdominal fat:

For men: Waist circumference ≥ 102 cm (40 in.)
For women: Waist circumference ≥ 88 cm (35 in.)

Note: The waist measurement is used to identify additional risk when BMI is between 18.5 and 34.9. For a BMI of 35.0 or more, the measurement is an unreliable indicator of health risk.

Source: Canadian Guidelines for Body Weight Classification in Adults, Health Canada, 2003.

A family perspective on weight

SPRING 2004

10

AHFMR RESEARCH NEWS

Obesity is no longer just a problem for adults. According to the latest research, it's an epidemic in children as well. A study published in 2004 by British researchers showed that children's waistlines have expanded by at least four centimetres—two clothing sizes—over the past 20 years. While some might wonder what is going on with kids, two University of Calgary nursing professors are taking a different approach. They're asking what is going on with families.

“We're using the family as the context for weight management,” says Dr. Lorraine Watson, who is working with Dr. Dianne Tapp on the project. “The family unit plays a significant role in establishing a child's eating and activity patterns. We have to understand weight management from a family perspective before we can develop programs that work for individuals.”

The team is looking at three groups of families (consisting of mother, father, and at least one child older than eight). One group will be made up of families in which at least one member is overweight and currently enrolled in Trim Gym, a weight-loss program offered at the University of Calgary. The second will include families in which one member has a self-identified weight problem, but does not attend a formal weight-loss program. The third group will consist of families where all members are of normal weight. Drs. Watson and Tapp hope to enrol a total of 45 families by the end of this year.

The study involves two sets of interviews with the entire family. Questions deal with issues such as food intake, activity levels, family members' perceptions of their health-risk factors, the degree to which work impinges on their ability to manage weight, and their feelings of connectedness to their community.

“Our goal with this study is to gain a solid understanding about how families look at weight management and what they do about it,” says Dr. Watson. “Our hope is that this knowledge can

then be used to design effective interventions that help families manage weight.”

Dr. Tapp notes that insights from this study could also be used in health-promotion activities, and as input for policy making. “As health professionals, we have a lot to learn from families—their challenges, their perspectives, and their successes. Our mission is to get this information and put it to work.”

If your family lives in the Calgary area and would be interested in participating in this study, call Dr. Watson at 220-6618 (or leave a message at 210-8840). ©

Dr. Lorraine Watson and Dr. Dianne Tapp are associate professors in the Faculty of Nursing at the University of Calgary. Their study, “Societal and Family Influences on Weight Management”, is funded by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Selected publication

Watson LA, Girard FM. Establishing integrity and avoiding methodological misunderstanding. *Qualitative Health Research*. In press 2004.

ABOVE: DR. DIANNE TAPP (L)
AND DR. LORRAINE WATSON (R)



The obesity epidemic

Fatty acylation of these proteins may lead to impaired energy metabolism.

One of Dr. Berthiaume's pioneering research projects is examining the fatty acylation of certain proteins in the mitochondria—the tiny energy factories inside our cells. Interestingly, fatty acylation of these proteins regulates their activity. Obese people have high levels of fatty acids in their blood. Dr. Berthiaume's team has preliminary data indicating that obesity also increases the fatty acylation of several proteins, and that many of these are in the mitochondria. Therefore, persistent increased fatty acylation of these proteins may lead to impaired energy metabolism. This important finding may help explain the altered metabolism of obese people, as well as the link between obesity and diabetes.

"The challenge now is to find more fatty-acylated proteins and understand their function," says Dr. Berthiaume. "It's not at all obvious which ones they are, so it requires painstaking research to isolate and characterize them. But we're in the right place at the right time, and we've developed the expertise to do this work."

Society's role

While medical scientists pursue the mysteries of cell signalling and metabolism in relation to obesity, another group of researchers is taking a different approach: social scientists are looking for answers outside the body. "We start from the premise that obesity rates have skyrocketed in the last 20 years, and ask why. Our genes haven't changed. Physically we're the same people. But our behaviour has most certainly changed—we eat more and we exercise less," says Heritage Scholar Dr. Kim Raine, director of the Centre for Health Promotion Studies at the University of Alberta.

"Many researchers, including myself, are interested in figuring out what is behind this change in behaviour. There is a multitude of contributing factors: the proliferation of fast-food restaurants; cities designed so that it makes more sense to



drive than walk; conveniences such as televisions and computers that encourage a sedentary lifestyle—and the list goes on. We need a systematic investigation to sort this out."

That is exactly what Dr. Raine has embarked upon. She leads a team of researchers that was recently awarded a \$1.5-million New Emerging Team (NET) grant by the Canadian Institutes of Health Research (CIHR). The five-year grant funds 17 projects designed to examine systematically the behavioural, environmental, and social causes of obesity. The team's mandate extends to developing public health strategies to promote healthy lifestyles and reduce obesity.

"Solutions to the problem of obesity have to go beyond simply trying to change individuals," says Dr. Raine. "The factors that influence obesity suggest that we need broader social and policy changes."

Dr. Raine's particular interest is the relationship between obesity and socio-economic status. Previous research has shown that the incidence of overweight and obesity is higher in low-income groups. One of Dr. Raine's current projects involves studying the accessibility of healthy food vs. unhealthy food, and the accessibility of recreational centres, parks, and trails in different

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The incidence of overweight and obesity is higher in low-income groups.

Active living— no matter what your age



DR. SANDY O'BRIEN COUSINS

Why do people get fatter as they get older? Exercise gerontologist Dr. Sandy O'Brien Cousins is looking for answers in the activity habits of elderly people. As people get older, there is a strong trend toward less physical activity.

"Activity is vital to maintaining muscle mass," says Dr. Cousins, a University of Alberta researcher who studies aging in physical-activity settings. Between the

ages of 25 and 50, most people lose about 10% of their muscle mass. Between the ages of 50 and 80, the decline is much higher—an additional 30%. Physical strength depends largely on muscle mass, which means that by 80 years of age inactive people are frail, whereas active people in the same age range are skiing, hiking, and enjoying life.

For women especially, loss of muscle goes hand in hand with a gain in fat. Elderly women who are not active often have a body weight that is 50% fat. Less muscle and more fat is a recipe for trouble—in the form of heart disease, cancer, diabetes, and chronic disorders.

Although hundreds of studies show the benefits of later-life exercise, more than half the population is underactive. Dr. Cousins' research is aimed at understanding why many older people think that vigorous physical activity is not appropriate for them. "The sad irony is that healthy people say they don't need to exercise, because they are already healthy, and the unhealthy people tell us they can't."

Part of the lack of motivation could be a poor "leisure ethic". Many older people do not see active leisure as essential to their health. They may also confuse being busy—playing bingo or doing crafts—with being active. "The key is having an active hobby like walking or bicycling that you enjoy doing," says Dr. Cousins.

She would also like to see incentives offered for active living—such as tax deductions for exercise expenses, free fitness tests, and longer lunch hours so that people could fit exercise into their day. "Community leaders need to look for creative ways to help citizens find enjoyable and affordable opportunities to age actively," she says. "It's a recipe for health." **en**

Dr. Sandy O'Brien Cousins is a full professor in the Faculty of Physical Education and Recreation at the University of Alberta. Her "Motivation for Later Life Activity" research is supported by the Social Sciences and Humanities Research Council (SSHRC).

The obesity epidemic

neighbourhoods in Edmonton. After identifying income-related variations in accessibility to neighbourhood healthy living resources, the team will examine the health levels of the people who live there. Dr. Raine hopes to be able to connect these data and learn something about how the environment affects obesity.

"The idea we're exploring is that there are 'obesogenic' environments: environments that promote obesity," she explains. "By changing something about these environments, we should be able to do something about obesity. Our ultimate goal is to promote healthy lifestyles by making the healthy choice the easy choice. That is social change."

Cree communities

Another researcher interested in social change is Dr. Noreen Willows, a member of Dr. Raine's New Emerging Team and a professor in the Faculty of Agriculture, Forestry and Home Economics at the University of Alberta. She has been engaged in the area of First Nations health for many years and her NET project examines child obesity in remote Cree communities in northern Quebec. "There's been a lot of research documenting the trend to larger children over the past 20 years," says Dr. Willows. "The same thing has happened to Aboriginal children. However, we suspect the conditions that predispose Aboriginal children to obesity may be somewhat different. This is what I'm exploring."



"We suspect the conditions that predispose Aboriginal children to obesity may be somewhat different."

Dr. Willows takes a community-based approach to research, in which community members and the researcher work together toward finding solutions to the problems inherent in the research topic. For her obesity project, Dr. Willows conducted detailed interviews with community members, asking them to identify the conditions which they believe promote obesity, as well as the particular strengths in the community that can work to keep their children healthy.

While the data collected last summer in three Cree communities are still being analyzed, Dr. Willows says one strong theme has already emerged. Many of the community members identified cultural loss as a key factor behind the obesity problem. They described how the loss of traditional values has led to general unwellness in the community, and talked about ways to strengthen traditional activities.

"We need to get a sophisticated understanding of the underlying causes of obesity in Aboriginal children from the perspective of the people who are facing this problem," says Dr. Willows. "It's the only way we'll be able to develop programs that are culturally sensitive and truly effective."

Losing weight to improve health

But the reality is that truly effective weight loss eludes more and more of us every day. And the costs are mounting. A 1999 Canadian study pegged the financial impact of obesity at a staggering \$1.8 billion for 1997 alone—the direct costs of only 10 obesity-related illnesses.

"It's not complicated. People are getting sick because they're too fat," says Dr. David Lau, a professor in the Faculty of Medicine at the University of Calgary, and director of the Julia McFarlane Diabetes Research Centre there. "We shouldn't be talking about losing weight to look better. We should be talking about losing weight to improve health."

He provides a graphic example: if individuals lose 5 to 10% of their body weight, they cut their risk of developing diabetes by 60%. "That's only 10 pounds for a 200-pound man," notes Dr. Lau. "People don't see the benefits of conservative weight loss. Instead, they set unrealistic goals, and set themselves up for failure."

Dr. Lau's growing sense of urgency about obesity is rooted in his research on factors that regulate fat-cell proliferation. "Fat cells are very active. They produce chemical messengers that act as mediators, changing how the body handles fat and sugars," he explains. "These mediators wreak havoc in the body."

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The epidemic

"We should be talking about losing weight to improve health."

They can alter the function of other fat cells, causing them to grow and multiply. They may be the culprits behind high blood pressure, cholesterol, and diabetes. In my lab we're looking for ways to turn off the production of these mediators."

As founding president of the non-profit group Obesity Canada, Dr. Lau has launched a call for action on obesity, urging all levels of government to implement effective strategies to combat the burgeoning epidemic. He thinks Alberta researchers have a key role to play. "In Alberta, we do excellent biomedical research related to obesity, as well as excellent population health and epidemiology research. We need to bring these areas together in an integrated way to understand what situational factors make people prone to obesity.

"Alberta is poised to become a leader in obesity research, in the same way we're on the forefront of diabetes research. There's a real opportunity here." 

Heritage Scientist Dr. William Colmers is a full professor in the Department of Pharmacology, part of the Faculty of Medicine and Dentistry at the University of Alberta. His research is supported by CIHR (the Canadian Institutes of Health Research), Merck & Co, and the National Institutes of Health (USA).

Heritage Scholar Dr. Richard Lehner is an assistant professor in the Department of Pediatrics and Child Health and the Department of Cell Biology, and a member of the CIHR Group on Molecular and Cell Biology of Lipids within the Faculty of Medicine and Dentistry at the University of Alberta. His research is supported by CIHR, the Heart and Stroke Foundation of Alberta, and GlaxoSmithKline.

Heritage Senior Scholar Dr. Luc Berthiaume is an associate professor in the Department of Cell Biology, part of the Faculty of Medicine and Dentistry at

the University of Alberta. His research is supported by CIHR, the Cancer Research Society, and the Heart and Stroke Foundation of Alberta.

Heritage Scholar Dr. Kim Raine is director of the Centre for Health Promotion Studies and a full professor in the Department of Agricultural, Food and Nutritional Science, part of the Faculty of Agriculture, Forestry and Home Economics at the University of Alberta. Her research is supported by CIHR, Alberta Health and Wellness, the Heart and Stroke Foundation of Canada, the Canadian Diabetes Association, and the Social Sciences and Humanities Research Council (SSHRC).

Heritage Population Health Investigator Dr. Noreen Willows is an assistant professor in the Department of Agricultural, Food and Nutritional Science at the University of Alberta. Her research is supported by CIHR, and she has also received support from the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. David Lau is a full professor in the departments of Medicine and Biochemistry and Molecular Biology, an adjunct professor in the Faculty of Kinesiology, and director of the Julia McFarlane Diabetes Research Centre at the University of Calgary. His research is also supported by the Heart and Stroke Foundation of Alberta and the University of Calgary.

Selected publications

Cowley MA, Smith RG, Diano S, Tschöp M, Pronchuk N, Grove KL, Strasburger CJ, Bidlingmaier M, Esterman M, Heiman ML, Garia-Segura LM, Nillni EA, Mendez P, Low MJ, Sotonyi P, Friedman JM, Liu H, Pinto S, Colmers WF, Cone RD, Horvath TL. Hypothalamic ghrelin acts presynaptically to regulate orexigenic circuits. *Neuron* 2003;37:649-661.

Gilham D, Ho S, Rasouli M, Martres P, Vance DE, Lehner R. Inhibitors of hepatic microsomal triacylglycerol hydrolase decrease very low density lipoprotein secretion. *FASEB Journal* 2003 Sep;17(12):1685-1687.

Corvi MM, Soltys C-LM, Berthiaume LG. Regulation of mitochondrial carbamoyl-phosphate synthetase 1 activity by active site fatty acylation. *Journal of Biological Chemistry* 2001 Dec 7;276(49):45704-45712.

Paquette M-C, Raine K. Sociocultural context of women's body image. *Social Science & Medicine*. In press 2004.

Doll M, Ball GDC, Willows ND. Rating of figures used for body image assessment varies depending on the method of figure presentation. *International Journal of Eating Disorders*. 2004;35(1):109-114.

Yan H, Kermouni A, Abdel-Hafez M, Lau DCW. Role of cyclooxygenases COX-1 and COX-2 in modulating adipogenesis in 3T3-L1 cells. *Journal of Lipid Research* 2003 Feb; 44(2):424-429.



Heritage Scholar Dr. Luis Schang does basic medical research on herpes simplex viruses to unlock the secrets of how they replicate and find new targets for antiviral drugs. But he started his working life in a slightly different field—veterinary medicine.

BLOCKING VIRUSES



Raised in Argentina, a major beef-producing country, Dr. Schang came from a long line of research veterinarians. "I think I followed the path by default," he

says. While studying veterinary medicine

at the National University of Buenos Aires, he dabbled in research on in vitro insemination and fertilization of cattle, later taking up research on foot-and-mouth disease while running a veterinary consultancy. "I realized that I really liked research, and I decided to go full-time," Dr. Schang says. "In Argentina, this basically means you have to leave the country, at least for some time, to complete your education."

Dr. Schang headed to the University of Nebraska-Lincoln in 1991, where he did his Ph.D. and post-doc studying two herpes viruses that produce significant diseases in farm animals. Whereas veterinary research was the way to go in cattle-rich Argentina, he soon realized that the resources in the US were in medical research. Applying his viral research to human herpes, he did four years of post-doctoral work at the University of Pennsylvania School of Medicine.

When it came time to look for a permanent position, Dr. Schang was very much attracted to the idea of raising his family in Canada but wasn't so sure he wanted to go as far north as the University of Alberta. Visiting the university for an interview sold him on the move. Getting laboratory start-up funds from AHFMR on top of his Canadian Institutes of Health Research (CIHR) grant sealed the deal because it gave him a level of support almost equal

to what he would have received in the US.

Dr. Schang's lab conducts basic research on human herpes simplex viruses (HSV) type 1 and 2. As with all viruses, herpes simplex only replicates inside cells, which it kills using cellular proteins (building blocks) to produce infectious viruses. Dr. Schang's group is interested in the roles that cellular proteins play in HSV replication. Certain cellular proteins, called cyclin-dependent kinases, are required for cell division and viral replication.

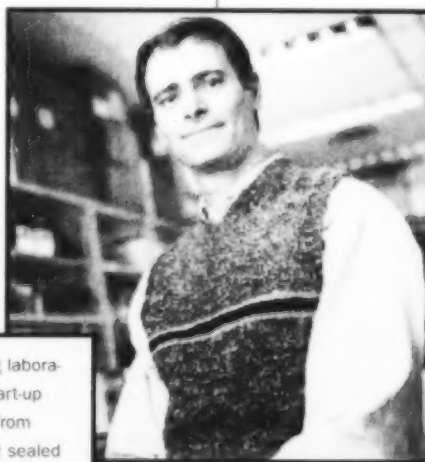
The team has discovered that drugs called pharmacological cyclin-dependent kinase inhibitors (PCIs) specifically block these proteins and exert powerful antiviral activity against HSV and HIV. Dr. Schang's group identified and characterized a previously unknown activity of these drugs: their ability to prevent gene expression. Although application of the basic research findings is still about a decade away, there could be many implications.

Other research teams are investigating PCIs as anti-cancer drugs, because of their ability to block cell growth, and as potential antivirals to combat several viruses, including HIV. **TM**

Heritage Scholar and CIHR New Investigator Dr. Luis M. Schang is an assistant professor in the Department of Biochemistry and the Department of Medical Microbiology and Immunology at the University of Alberta.

Selected publication

Schang LM, Bantly A, Knockaert M, Shaheen F, Meijer L, Malim MH, Gray NS, Schaffer PA. Pharmacological cyclin-dependent kinase inhibitors inhibit replication of wild-type and drug-resistant strains of herpes simplex virus and human immunodeficiency virus type 1 by targeting cellular, not viral, proteins. *Journal of Virology* 2002 Aug; 76(15):7874-7882.



Getting laboratory start-up funds from AHFMR sealed the deal.

ABOVE: DR. LUIS SCHANG

THE MECHANISMS OF

pain

AND

inflammation



We all know that when we injure ourselves, we experience pain and inflammation (heat, swelling, and redness). These are the body's responses to injury, and the first signs

that there is a problem. But what AHFMR Scholar Dr. Nathalie Vergnolle wants to know is this: What makes it happen? What are the mechanisms involved?



One mechanism involves proteinases (molecules that digest other molecules). Dr. Vergnolle explains that for many years, scientists thought proteinases simply acted as scavengers, cleaning the inflammation sites. Then, about ten years ago, it was revealed that the proteinases actually signal to the cell by activating receptors (structures on the surface or interior of a cell that selectively receive and bind specific substances). Since that time, four specific proteinase-activated receptors have been discovered. Dr. Vergnolle wants to find out which of our body's proteinases activate these receptors, and what happens in terms of pain and inflammation when the receptors are triggered.

"We have shown that one of those four receptors is actually present on the nerves where it sends a message of pain when activated," says Dr. Vergnolle. "This activation is crucial to the generation of pain and all the symptoms associated with it. If we block this receptor, it could have implications for developing new painkillers."

LEFT: DR. NATHALIE VERGNOLLE



Some of the other receptors, however, behave differently when activated: they seem to reduce pain rather than initiating it. Instead of blocking these receptors, then, it would be better to develop a means of triggering them. Acting on receptors at the site of injury is an innovative approach—most painkillers for moderate pain currently on the market act on the central nervous system and the perception of pain.

The receptors involved in pain are also present in inflammation: their activation causes the inflammatory reaction. The challenge is to learn whether there is a crucial event during the reaction that can lead to a chronic inflammatory condition, such as arthritis

“If we block this receptor, it could have implications for developing new painkillers.”

or inflammatory bowel disease. “Inflammation itself is a good thing,” explains Dr. Vergnolle. “But in some cases it becomes uncontrolled, and that is where you want to diminish it.” The aim is to understand whether those receptors and the proteinases that activate them are involved in this transition from a normal inflammatory response to the sort of uncontrolled response that leads to a more chronic state of pain.

Dr. Vergnolle came to Calgary in 1997 from her native France to do a post-doc with Heritage Scientist Dr. John Wallace, with whom she continues to collaborate on some aspects of her research. Because her work on pain and inflammation has the potential for many applications, Dr. Vergnolle also collaborates with a number of other Heritage researchers at the University of Calgary, who study such conditions as multiple sclerosis, inflammatory bowel disease, Crohn’s disease, arthritis, and diabetes. “There has been a lot of interest in this work,” she says. **MD**

Dr. Nathalie Vergnolle is an AHFMR Scholar and an assistant professor in the University of Calgary’s Department of Pharmacology and Therapeutics. She also receives funding from the Canadian Institutes of Health Research (CIHR), the Crohn’s and Colitis Foundation of Canada, and the Canadian Association of Gastroenterology.

Selected publications

Vergnolle N. The enteric nervous system in inflammation and pain: the role of proteinase-activated receptors. *Canadian Journal of*

Gastroenterology 2003 Oct;17(10):589-592.

Vergnolle N, Ferazzini M, D’Andrea MR, Buddenkotte J, Steinhoff M. Proteinase-activated receptors: novel signals for peripheral nerves. *Trends in Neurosciences* 2003 Sep;26(9):496-500.

Vergnolle N, Bunnett NW, Sharkey KA, Brussee V, Compton SJ, Grady EF, Cirino G, Gerard N, Basbaum AI, Andrade-Gordon P, Hollenberg MD, Wallace JL. Proteinase-activated receptor 2 and hyperalgesia: a novel pain pathway. *Nature Medicine* 2001 Jul;7(7):821-826.



There aren't any glossy brochures touting potential hepatitis and cancer treatments in the offices of Edmonton biotechnology company ViRexx Medical Corp. Why not? It's a case of "been there, done that" for ViRexx President and CEO Dr. Tony Noujaim. One of the lessons he has learned in his 20 years in the biotech industry is "save the dollars for the real stuff."

Harnessing the body's *heal*

So although the company has been around since 1999 and has 23 employees, ViRexx has been keeping a low public profile. But that's all about to change. ViRexx is trading on the TSX Venture Exchange and, says Dr. Noujaim, "now is the time to talk. Things are coming together for us after a lot of hard work."

ViRexx has two main technology platforms, both of which harness the body's natural ability to heal itself. One, called Chimigen, directs the immune system to recognize and destroy specific disease-causing agents in the body. The initial focus is on therapies for chronic hepatitis B and hepatitis C infections. The immune systems of many people exposed to these viruses do not respond and cannot ward off the disease. These individuals develop tolerance to the virus and become chronic carriers of the disease.

Hepatitis B (HBV) and hepatitis C (HCV) are serious global health problems. The World Health Organization estimates that one of every three people in the world has been infected with HBV, and of that group approximately 350 million have developed a chronic HBV infection. About 170 million people are

chronically infected with HCV, and between 3 million and 4 million are newly infected each year. Chronically infected persons are at high risk of death from liver cancer and cirrhosis of the liver.

While antiviral drugs to treat hepatitis exist, the viruses often mutate into forms that are resistant to the therapies. ViRexx is developing two vaccines based on the Chimigen technology—HepaVaxx B and HepaVaxx C. These are "therapeutic vaccines", administered after a person has the infection. HepaVaxx B is about a year away from clinical trials; HepaVaxx C will begin trials in about two years.

ViRexx's second technology platform is T-ACT, which stands for "targeted autothrombogenic cancer therapy", the technical description of a way to cut off the blood supply to tumours. ViRexx's lead product based on T-ACT is called Occlusin. Delivered by catheter to the main vessel feeding the tumour, it physically cuts off the blood supply by means of a clot. This deprives the cancer cells of the oxygen and nutrients they need to survive. Even limited damage to the tumour's vascular system has the potential to produce extensive tumour-cell death.

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**ViRexx
has two main
technology
platforms.**

"We're very excited about the potential of our technologies to treat a range of diseases."

ing abilities

The first target for Occlusin is liver tumours.

"Hepatitis B and C infections frequently result in liver cancer," explains Dr. Noujaim. "ViRexx products target the spectrum of conditions caused by these viruses: the infection itself (with products based on Chimigen) as well as one of the serious consequences—liver cancer (with Occlusin)."

Occlusin will enter Phase 1 clinical trials in the third quarter of this year. "We know that we can induce a clot with Occlusin, use it to block a blood vessel, shrink the tumour, and ensure that the clot remains where we want it," says Dr. Noujaim. "Our challenge now is to prove this in clinical trials."

Enter AHFMR's Technology Commercialization (TC) program. ViRexx has received TC funding to support Phase 1 clinical trials for Occlusin. "The TC funding came at a critical stage for us. It helps us move forward, and this is essential to enhancing shareholder value," says Mike Stewart, ViRexx Vice-President of Drug Development and co-inventor of the T-ACT technology. "In addition, the peer-review process that we had to go through to obtain the TC funding adds credibility to our project. Investors pay attention to this."

Besides its use as a potential treatment for the type of liver cancer that develops as a result of chronic hepatitis infection, Occlusin could also be

used to treat other forms of liver cancer. In the United States, the five-year survival rate for patients with all stages of liver cancer is 6%. There has been little improvement in the survival rate over the past 30 years.

Another potential target for Occlusin is uterine fibroids—non-malignant growths in the wall of the uterus. Approximately 30% to 40% of women over the age of 30 have fibroids. About 20% of these women experience severe, debilitating symptoms, such as heavy bleeding, anemia, and pelvic pain.

"We're very excited about the potential of our technologies to treat a range of diseases, although we know there's a long way yet to go," says Dr. Noujaim. And in the pharmaceutical business, a long way means a lot of money. That's another one of Dr. Noujaim's lessons—always have a financial cushion—learned from his experience as founder of two Alberta biotech companies, Biomira and AltaRex.

He says that ViRexx has enough money in the bank to support two to three years of operations. "We're aiming for conservative growth of the company. I don't want to get big and then shrink. My vision is that by 2007 ViRexx will be the number one biotech company in Canada."

"This is a glorious opportunity to capitalize on major breakthroughs in science that have come from Alberta labs. We're creating high-quality jobs, establishing a cluster of biotech-related businesses, creating wealth for investors, and growing an Alberta-based biotech industry that is global in scope." ■



Babies on treadmills

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AHMR RESEARCH NEWS



"Never work with children or animals," advises a well known showbiz proverb. Not so in the research world, however, where animals have taught us a great deal. And now neuroscience master's student Kristin Musselman is learning from babies—babies on treadmills, in fact.

Long before they ever take their first real steps, infants possess a stepping response—their legs make automatic stepping movements when their weight is supported. At this point in their lives the higher centres of the brain that control locomotion have not yet matured, so it seems that the stepping response is controlled by the brain stem or spinal cord. "But we're not entirely sure yet what's happening there in terms of the circuitry that controls the stepping," says Kristin. Although the stepping response is present at birth, for some reason it is not typically exhibited between the ages of three and six months. "Within that window of time, we're trying to come up with ways to elicit the stepping."

Kristin works with Dr. Jaynie Yang in the Faculty of Rehabilitation Medicine at the University of Alberta. While conducting treadmill therapy on adult patients with spinal cord injuries, Dr. Yang observed an involuntary stepping similar to that of the babies, particularly in those patients with only partial lesions to their spinal cords. Understanding how the stepping circuitry works in babies and discovering how to trigger the stepping could one day lead to the development of better therapies for movement training in such patients.

The stepping response is controlled by the brain stem or spinal cord.



Kristin and Dr. Yang conduct their studies in the most child-friendly lab you are ever likely to see. The room is dominated by two treadmills decorated with brightly coloured, plush baby toys. The babies in the study (their parents are recruited at public-health clinics) are placed on the treadmills, with parents or lab members supporting their weight. Markers and electrodes are attached to their legs to digitize and record their movements. Grasping toys, they happily step away, paying little attention to the treadmill direction or speed. "The babies seem to love it," says


ABOVE: KRISTIN MUSSELMAN (L) AND DR. JAYNIE YANG (R)



"The babies seem to love it."

Kristin. "They walk in whatever direction you turn them—forward, backward, sideways."

One of the treadmills has two separate, parallel belts, which can be set at different speeds for each leg, or with one belt going backward and one forward. This doesn't faze the babies either. "There is not a single command telling them to walk," explains Dr. Yang. "The two legs are driven by separate sensory input coming into the legs."

Kristin completed her undergraduate work in physical therapy at Queen's University in Kingston, Ontario. Her interest in neurological rehabilitation was triggered while working as a physiotherapist with stroke patients. Pursuing that interest brought her to Alberta in September 2003 to work with Dr. Yang. "My research is one piece of the neuro-rehab puzzle," says Kristin. 

Kristin Musselman receives funding through a training partnership between AHFMR and Neuroscience Canada. She is a master's student at the Centre for Neuroscience, University of Alberta.

Dr. Jaynie Yang is an associate professor in the Department of Physical Therapy, part of the Faculty of Rehabilitation Medicine at the University of Alberta. She receives funding from CIHR and NSERC.

Selected publications

Yang JF, Lam T, Pang MYC, Lamont E, Musselman K, Seinen E. Infant stepping: a window to the behaviour of the human pattern generator for walking. *Canadian Journal of Physiology and Pharmacology*. Submitted 2004.

Lam T, Wolstenholme C, van der Linden M, Pang MYC, Yang JF. Stumbling corrective responses during treadmill-elicited stepping in human infants. *Journal of Physiology* 2003 Nov;553(1):319-331.

reader resources



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The fitness habit

Alberta Centre for Active Living
<http://www.centre4activeliving.ca>

Fighting cancer with fitness

University of Calgary Department of Oncology
<http://www.med.ucalgary.ca/webs/oncology/>

University of Calgary Faculty of Kinesiology
<http://www.kin.ucalgary.ca>

The obesity epidemic

CIHR Group in Molecular and Cell Biology of Lipids
<http://cihr-mcblgroup.org/>

Dr. Luc Berthiaume's web site
<http://www.ualberta.ca/CELLBIOLOGY/berthiaume.html>

Centre for Health Promotion Studies
<http://www.chps.ualberta.ca>

Am I overweight?

Health Canada Office of Nutrition Policy and Promotion
<http://www.healthcanada.ca/nutrition>

Active living—no matter what your age

Health Canada Physical Activity Guide
<http://www.paguide.com>

Active Living Coalition for Older Adults
<http://www.alcoa.ca>

International Society for Aging and Physical Activity
<http://www.isapa.org>

The mechanisms of pain and inflammation

University of Calgary Mucosal Inflammation Research Group
<http://www.ucalgary.ca/~migr/>

Harnessing the body's healing abilities

VIRExx Medical Corp
<http://www.virexx.com>

AHFMR announces \$22 million for health research

Last September, 50-year-old Marv Lipka suffered a profound stroke in the high left front part of his brain. It left him mute and paralyzed on the right side of his body.

Marv received excellent care after his stroke and participates in intensive therapy three times a week.

Marv is an enthusiastic advocate of Heritage Senior Scholar Dr. Jeffrey Kleim's investigations into the post-stroke brain. Dr. Kleim's ground-breaking stroke research at the University of Lethbridge has earned him funding this year from the Alberta Heritage Foundation for Medical Research (AHFMR). Dr. Kleim is one of 40 researchers across the province who were successful in AHFMR's 2004 competition. This year, AHFMR offered \$22 million in grants to researchers at the universities of Lethbridge, Calgary, and Alberta.

AHFMR funding provides salaries, equipment, laboratory start-up, and other support for top health researchers in our province. Over the past five years



AHFMR has invested more than \$240 million in health research in Alberta.

The following researchers have been offered AHFMR funding this year:

Colin Anderson (diabetes) UA
David Brindley (cancer) UA
Alastair Buchan (stroke) UC
Alexander Clark (heart health) UA
William Colmers (obesity/epilepsy) UA
Nicholas Coupland (depression) UA
David Evans (viral disease) UA
Jeffrey Gaudet (organ formation) UC
Sita Gourishankar (kidney disease/transplantation) UA
Roy Gravel (genetic disorders) UC
Kevin Hildebrand (joints and bones) UC
Robert Hilsden (digestive tract screening) UC
Jeffrey Johnson (diabetes care) UA
Satyabrata Kar (Alzheimer's disease) UA
Jeffrey Kleim (stroke) UL
Ernest Lam (oral cancer) UA

ABOVE: DR. JEFFREY KLEIM (L)
WITH MARV LIPKA

Richard Lehner (cholesterol) UA
Ki-Young Lee (brain development) UC
Ian Lo (joints and tendons) UC
Rodger Loutzenhiser (kidney) UC
Karen Madsen (Crohn's disease) UA
Paul Mains (embryo development) UC
Sumit Majumdar (improving quality of care) UA
Ronald Moore (bladder cancer) UA
Ian Parney (brain cancer) UC
Scott Patten (mental illness) UC
Ronald Plotnikoff (physical activity) UA
Hude Quan (healthcare delivery) UC
Derrick Rancourt (genetics and fertility) UC
Linda Reha-Krantz (genetics) UA
Jana Rieger (cancer rehabilitation) UA
David Schriemer (improving drug design) UC
James Shapiro (diabetes) UA
Mark Swain (liver) UC
Hendrik ter Keurs (heart failure) UC
John Wallace (pain and inflammation) UC
Noreen Willows (obesity in children) UA
Richard Wilson (sleep apnea/SIDS) UC
Brent Winston (response to infection) UC
Richard Wozniak (genetics) UA

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Write:

Alberta Heritage Foundation
for Medical Research
1500, 10104 - 103 Avenue
Edmonton, Alberta T5J 4A7

Physicians: please place in your patient waiting rooms.



AHFMR announces \$22 million for health research

SPRING 2004

22

AHFMR RESEARCH NEWS

Marv received excellent care after his stroke and participates in intensive therapy three times a week.

Marv is an enthusiastic advocate of Heritage Senior Scholar Dr. Jeffrey Kleim's investigations into the post-stroke brain. Dr. Kleim's ground-breaking stroke research at the University of Lethbridge has earned him funding this year from the Alberta Heritage Foundation for Medical Research (AHFMR). Dr. Kleim is one of 40 researchers across the province who were successful in AHFMR's 2004 competition. This year, AHFMR offered \$22 million in grants to researchers at the universities of Lethbridge, Calgary, and Alberta.


AHFMR funding provides salaries, equipment, laboratory start-up, and other support for top health researchers in our province. Over the past five years



AHFMR has invested more than \$240 million in health research in Alberta.

The following researchers have been offered AHFMR funding this year:

Colin Anderson (diabetes) UA
David Brindley (cancer) UA
Alastair Buchan (stroke) UC
Alexander Clark (heart health) UA
William Colmers (obesity/epilepsy) UA
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